

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claims 1-15 (Cancelled).

16. (Currently Amended) An isolated nucleic acid comprising a nucleotide sequence encoding the effector domain of the binding molecule as claimed in claim 32, wherein said nucleic acid is DNA.

17. (Currently Amended) An isolated nucleic acid comprising a nucleotide sequence encoding a the binding molecule as claimed in claim 32, wherein said nucleic acid is DNA.

18. (Currently Amended) A The nucleic acid as claimed in claim 16 which is a replicable vector.

19. (Currently Amended) A The nucleic acid as claimed in claim 18 wherein the nucleotide sequence is operably linked to a promoter.

20. (Previously Presented) A host cell comprising or transformed with the vector of claim 19.

21. (Currently Amended) A process for producing a binding molecule ~~as claimed in claim 32,~~ which is a recombinant polypeptide comprising:

(i) a binding domain capable of binding a target molecule, which binding domain is the binding site of an antibody, and

(ii) an effector domain having an amino acid sequence homologous to a constant domain of a human immunoglobulin heavy chain;

wherein the binding molecule is capable of binding the target molecule without triggering significant complement dependent lysis, or cell mediated destruction of the target, and the effector domain is capable of specifically binding FcγRIIb and optionally FcRn,

and wherein the effector domain comprises a chimeric C_H2 domain which is derived from two or more human immunoglobulin heavy chain C_H2 domains, which human immunoglobulins are selected from IgG1, IgG2 and IgG4,

and wherein the effector domain has a reduced affinity for FcγRI, FcγRIIa and FcγRIII and a reduced ability to mediate complement lysis by comparison with said constant domain of a human immunoglobulin heavy chain;

the process comprising the step of modifying a nucleotide sequence encoding a first human immunoglobulin heavy chain C_H2 domain such that 2, 3 or 4 amino acids in at least 1 region of the C_H2 domain ~~corresponds~~ correspond to ~~the an~~ amino acids from a second human immunoglobulin heavy chain C_H2 domain,

~~wherein the region is selected from the 2 discrete regions numbered residues 233-236, and 327-331 in accordance with the EU numbering system,~~

wherein said modification introduces the following blocks of amino acids at the stated positions: 233P, 234V, 235A, 236G, 327G, 330S and 331S numbered with respect to the EU numbering system of Kabat

and wherein in ~~each case the human immunoglobulin is selected from IgG1, IgG2 and IgG4~~ said chimeric C_H2 domain is at least 98% identical to a C_H2 sequence (residues 231-340) from human IgG1 or IgG4 having said modified amino acids.

22. (Currently Amended) ~~A~~ The process as claimed in claim 21 wherein 2 amino acids in 1 region of the C_H2 domain are modified to the corresponding amino acids from a the second human immunoglobulin heavy chain C_H2 domain.

23. (Previously Presented) A method of binding a target molecule comprising contacting said target molecule with a binding molecule of claim 32 under conditions allowing binding.

24. (Currently Amended) ~~A~~ The method of claim 23 wherein the target molecule is FcγRIIb, which binding causes inhibition of one or more of: B cell activation; mast cell degranulation; phagocytosis.

25. (Currently Amended) ~~A~~ The method of claim 24 to prevent, inhibit, or otherwise interfere with the binding of a second binding molecule to the target molecule.

26. (Currently Amended) ~~A~~ The method of claim 25 wherein the second binding molecule is an antibody.

27. (Currently Amended) ~~A~~ The method of claim 25 wherein the target molecule is selected from: the RhD antigen of red blood cells; an HPA alloantigen of platelets; a neutrophil antigen; a T-cell receptor; integrin; GBM collagen; Der P1; HPA-1a; VAP-1; laminin; lutheran; platelet glycoprotein VI; platelet glycoprotein Ia/IIa.

28. (Currently Amended) ~~A~~ The method of claim 24 for the treatment of a patient for a disorder selected from: Graft-vs-host disease; host-vs-graft disease; organ transplant rejection; bone-marrow transplant rejection; autoimmunity such as vasculitis, autoimmune haemolytic anaemia, autoimmune thrombocytopenia and arthritis; alloimmunity such as foetal/neonatal alloimmune thrombocytopenia; asthma and allergy; chronic or acute inflammatory diseases such as Chrohn's; HDN; Goodpastures, sickle cell anaemia, coronary artery occlusion.

29. (Currently Amended) ~~A~~ The method of claim 23 wherein the binding molecule is administered to a patient, or optionally in cases where the patient is an unborn infant, to the mother of the patient.

Claim 30 (Canceled).

31. (Withdrawn and Currently Amended) An oligonucleotide selected from:
MO22BACK: 5' TCT CCA ACA AAG GCC TCC CGT CCT CCA TCG AGA AAA 3' (SEQ ID
NO:16)

MO22: 5' TTT TCT CGA TGG AGG ACG GGA GGC CTT TGT TGG AGA 3' (SEQ ID

NO:17)

MO7BACK: 5' TCC TCA GCA CCT CCA GTC GCG GGG GGA CCG TCA GTC 3' (SEQ ID

NO:18)

MO21: 5' GAC TGA CGG TCC CGC GAC TGG AGG TGC TGA GGA 3' (SEQ ID NO:19)

32. (Currently Amended) A binding molecule which is a recombinant polypeptide comprising:

(i) a binding domain capable of binding a target molecule, which binding domain is the binding site of an antibody, and

(ii) an effector domain having an amino acid sequence homologous to ~~all or part of~~ a constant domain of a human immunoglobulin heavy chain;

wherein the binding molecule is capable of binding the target molecule without triggering significant complement dependent lysis, or cell mediated destruction of the target, and the effector domain is capable of specifically binding FcγRIIb and optionally FcRn,

and wherein the effector domain is comprises a chimeric C_H2 domain which is derived from two or more human immunoglobulin heavy chain ~~C_H2~~ C_H2 domains, which human immunoglobulins are selected from IgG1, IgG2 and IgG4,

and wherein the effector domain has a reduced affinity for FcγRI, FcγRIIa and FcγRIII and a reduced ability to mediate complement lysis by comparison with said constant domain of a human immunoglobulin heavy chain ~~C_H2-domains~~

and wherein the chimeric C_H2 domain is a human immunoglobulin heavy chain ~~C_H2~~ C_H2 domain which has the following blocks of amino acids at the stated positions: 233P, 234V,

235A₁ and 236G₁ and 327G, 330S and 331S numbered with respect to the EU numbering system of Kabat, and is at least 98% identical to a C_H2 sequence (residues 231-340) from human IgG1 or IgG4 having said modified amino acids.

33. (Currently Amended) The binding molecule as claimed in claim 32 wherein the effector chimeric C_H2 domain ~~is selected from~~ comprises G1Δac (SEQ ID NO:3) or G4Δc (SEQ ID NO:12) as shown in Figure 17.

Claim 34. (Cancelled)

Claim 35. (Cancel).

Claim 36. (Cancelled)

37. (Previously Presented) The binding molecule as claimed in claim 32 wherein the binding domain derives from a different source to the effector domain.

38. (Previously Presented) The binding molecule as claimed in claim 32 wherein the binding domain is capable of binding any of: the RhD antigen of red blood cells; an HPA alloantigen of platelets; a neutrophil antigen; a T-cell receptor; integrin; GBM collagen; Der P1; HPA-1a; VAP-1; laminin; lutheran; platelet glycoprotein VI; platelet glycoprotein Ia/IIa.

39. (Currently Amended) The binding molecule as claimed in claim 38 wherein the binding domain is selected from ~~that of~~ anti-CD52 antigen found on human lymphocytes; ~~FOG1; OKT3; B2 (anti-HPA-1a); VAP-1; murine anti- α 3 (IV) NC1; YTH12.5 (CD3); 2C7 (anti-Der p1); anti-laminin; or anti-lutheran~~ anti-RhD; anti-HPA-1a; anti-VAP-1; murine anti- α 3 (IV) NC1; anti-CD3; anti-Der p I; anti-laminin; anti-lutheran.

40. (Previously Presented) A pharmaceutical preparation comprising a binding molecule as claimed in claim 32 plus a pharmaceutically acceptable carrier.

41. (Currently Amended) A binding molecule which is a recombinant polypeptide comprising:

(i) a binding domain capable of binding a target molecule, which binding domain is the binding site of an antibody, and

(ii) an effector domain having an amino acid sequence homologous to ~~all or part of~~ a constant domain of a human immunoglobulin heavy chain;

wherein the binding molecule is capable of binding the target molecule without triggering significant complement dependent lysis, or cell mediated destruction of the target, and the effector domain is capable of specifically binding Fc γ RIIb and optionally FcRn,

and wherein the effector domain is comprises a chimeric C_H2 domain which is derived from two or more human immunoglobulin heavy chain ~~CH2~~ C_H2 domains, which human immunoglobulins are selected from IgG1, IgG2 and IgG4,

and wherein the effector domain has a reduced affinity for FcγRI, FcγRIIa and FcγRIII and a reduced ability to mediate complement lysis by comparison with said constant domain of a human immunoglobulin heavy chain C_H2 domains

and wherein the chimeric C_H2 domain is a human immunoglobulin heavy chain ~~CH2~~ C_H2 domain which has the following blocks of amino acids at the stated positions: 233P, 234V, 235A and no residue at 236₂, ~~and~~ 327G, 330S and 331S, numbered with respect to the EU system of Kabat, and is at least 98% identical to a ~~CH2~~ C_H2 sequence (residues 231-340) from human IgG1 or IgG2 having said modified amino acids.

42. (Currently Amended) The binding molecule as claimed in claim 41 wherein the chimeric C_H2 ~~effector domain is selected from~~ comprises G1Δab (SEQ ID NO:1) or G2Δa (SEQ ID NO:2) as shown in Figure 17.

Claim 43. (Cancelled)

Claim 44. (Cancel).

Claim 45. (Cancelled)

46. (Previously Presented) The binding molecule as claimed in claim 41 wherein the binding domain derives from a different source to the effector domain.

47. (Previously Presented) The binding molecule as claimed in claim 41 wherein the binding domain is capable of binding any of: the RhD antigen of red blood cells; an HPA alloantigen of platelets; a neutrophil antigen; a T-cell receptor; integrin; GBM collagen; Der P1; HPA-1a; VAP-1; laminin; lutheran; platelet glycoprotein VI; platelet glycoprotein Ia/IIa.

48. (Currently Amended) The binding molecule as claimed in claim 47 wherein the binding domain is selected from that of anti-CD52 antigen found on human lymphocytes; ~~FOG1; OKT3; B2 (anti-HPA-1a); VAP-1; murine anti- α 3 (IV) NC1; YTH12.5 (CD3); 2C7 (anti-Der p I); anti-laminin; anti-lutheran~~ anti-RhD; anti-HPA-1a; anti-VAP-1; murine anti- α 3 (IV) NC1; anti-CD3; anti-Der p I; anti-laminin; anti-lutheran.

49. (Previously Presented) A pharmaceutical preparation comprising a binding molecule as claimed in claim 41 plus a pharmaceutically acceptable carrier.

50. (New) An isolated nucleic acid comprising a nucleotide sequence encoding the effector domain of the binding molecule as claimed in claim 41, wherein said nucleic acid is DNA.

51. (New) An isolated nucleic acid comprising a nucleotide sequence encoding the binding molecule as claimed in claim 41, wherein said nucleic acid is DNA.

52. (New) The nucleic acid as claimed in claim 50 which is a replicable vector.

53. (New) The nucleic acid as claimed in claim 52 wherein the nucleotide sequence is operably linked to a promoter.

54. (New) A host cell comprising or transformed with the vector of claim 53.

55. (New) A process for producing a binding molecule which is a recombinant polypeptide comprising:

- (i) a binding domain capable of binding a target molecule, which binding domain is the binding site of an antibody, and
- (ii) an effector domain having an amino acid sequence homologous to a constant domain of a human immunoglobulin heavy chain;

wherein the binding molecule is capable of binding the target molecule without triggering significant complement dependent lysis, or cell mediated destruction of the target, and the effector domain is capable of specifically binding Fc γ RIIb and optionally FcRn,

and wherein the effector domain comprises a chimeric C_H2 domain which is derived from two or more human immunoglobulin heavy chain C_H2 domains, which human immunoglobulins are selected from IgG1, IgG2 and IgG4,

and wherein the effector domain has a reduced affinity for Fc γ RI, Fc γ RIIa and Fc γ RIII and a reduced ability to mediate complement lysis by comparison with said constant domain of a human immunoglobulin heavy chain;

the process comprising the step of modifying a nucleotide sequence encoding a first human immunoglobulin heavy chain C_H2 domain such that 2, 3 or 4 amino acids in at least 1

region of the C_H2 domain correspond to the amino acids from a second human immunoglobulin heavy chain C_H2 domain,

wherein said modification introduces the following blocks of amino acids at the stated positions: 233P, 234V, 235A, 236G, 327G, 330S and 331S numbered with respect to the EU numbering system of Kabat

and wherein in said chimeric C_H2 domain is at least 98% identical to a C_H2 sequence (residues 231-340) from human IgG1 or IgG4 having said modified amino acids.

56. (New) The process as claimed in claim 55 wherein 2 amino acids in 1 region of the C_H2 domain are modified to the corresponding amino acids from the second human immunoglobulin heavy chain C_H2 domain.

57. (New) A method of binding a target molecule comprising contacting said target molecule with a binding molecule of claim 41 under conditions allowing binding.

58. (New) The method of claim 57 wherein the target molecule is FcγRIIb, which binding causes inhibition of one or more of: B cell activation; mast cell degranulation; phagocytosis.

59. (New) The method of claim 58 to prevent, inhibit, or otherwise interfere with the binding of a second binding molecule to the target molecule.

60. (New) The method of claim 59 wherein the second binding molecule is an antibody.

61. (New) The method of claim 59 wherein the target molecule is selected from: the RhD antigen of red blood cells; an HPA alloantigen of platelets; a neutrophil antigen; a T-cell receptor; integrin; GBM collagen; Der P1; HPA-1a; VAP-1; laminin; lutheran; platelet glycoprotein VI; platelet glycoprotein Ia/IIa.

62. (New) The method of claim 58 for the treatment of a patient for a disorder selected from: Graft-vs-host disease; host-vs-graft disease; organ transplant rejection; bone-marrow transplant rejection; autoimmunity such as vasculitis, autoimmune haemolytic anaemia, autoimmune thrombocytopenia and arthritis; alloimmunity such as foetal/neonatal alloimmune thrombocytopenia; asthma and allergy; chronic or acute inflammatory diseases such as Chrohn's; HDN; Goodpastures, sickle cell anaemia, coronary artery occlusion.

63. (New) The method of claim 57 wherein the binding molecule is administered to a patient, or optionally in cases where the patient is an unborn infant, to the mother of the patient.

64. (new) The binding molecule as claimed in claim 39 wherein the anti-CD52 binding domain is CAMPATH-1; the anti-RhD is FOG1; the anti-Der p I is 2C7; the anti-CD3 is YTH12.5.

65. (new) The binding molecule as claimed in claim 48 wherein the anti-CD52 binding domain is CAMPATH-1; the anti-RhD is FOG1; the anti-Der p I is 2C7; the anti-CD3 is YTH12.5.

66. (new) A process for producing a binding molecule which is a recombinant polypeptide comprising:

(i) a binding domain capable of binding a target molecule, which binding domain is the binding site of an antibody, and

(ii) an effector domain having an amino acid sequence homologous to a constant domain of a human immunoglobulin heavy chain;

wherein the binding molecule is capable of binding the target molecule without triggering significant complement dependent lysis, or cell mediated destruction of the target, and the effector domain is capable of specifically binding FcγRIIb and optionally FcRn,

and wherein the effector domain comprises a chimeric C_H2 domain which is derived from two or more human immunoglobulin heavy chain C_H2 domains, which human immunoglobulins are selected from IgG1, IgG2 and IgG4,

and wherein the effector domain has a reduced affinity for FcγRI, FcγRIIa and FcγRIII and a reduced ability to mediate complement lysis by comparison with said constant domain of a human immunoglobulin heavy chain;

the process comprising the step of modifying a nucleotide sequence encoding a first human immunoglobulin heavy chain C_H2 domain such that 2, 3 or 4 amino acids in at least 1 region of the C_H2 domain correspond to the amino acids from a second human immunoglobulin heavy chain C_H2 domain,

wherein said modification introduces the following blocks of amino acids at the stated positions: 233P, 234V, 235A and no residue at 236, 327G, 330S and 331S numbered with respect to the EU numbering system of Kabat

and wherein said chimeric C_H2 domain is at least 98% identical to a C_H2 sequence (residues 231-340) from human IgG1 or IgG2 having said modified amino acids,

67. (new) The process as claimed in claim 66 wherein 2 amino acids in 1 region of the C_H2 domain are modified to the corresponding amino acids from the second human immunoglobulin heavy chain C_H2 domain.